

Allergic Contact Dermatitis from 12-Hydroxystearic Acid and Hydrogenated Castor Oil

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A 34-year-old male experienced severe allergic contact dermatitis from 12-hydroxystearic acid in a lip balm and from hydrogenated castor oil in an underarm deodorant. He also had a positive patch-test reaction to bis-diglyceryl polyacyladipate-2, which is present in the implicated lip balm and which itself contains 12-hydroxystearic acid. He was also incidentally found to have contact allergy to ricinoleic acid and castor oil. Ricinoleic acid is the principal fatty acid in castor oil, whereas 12-hydroxystearic acid is the principal fatty acid in hydrogenated castor oil. These two fatty acids are each 18-carbon 12-hydroxylated fatty acids, differing only in degree of saturation. The lack of patch-test reactivity to the analogous nonhydroxylated fatty acids, stearic acid (C18:0), and oleic acid (C18:1) indicates that 12-hydroxylation was required for allergenicity in this patient. In addition, serial dilution testing demonstrated that saturation of the hydroxylated C18 fatty acid enhanced its allergenicity.

THE CASTOR PLANT, *Ricinus communis*, grows in warm temperate regions throughout much of the world. Pressing and solvent extraction of castor seeds (often called beans) yield castor oil and a residual meal, also called mash or cake. The meal (but not the oil) contains the toxic alkaloid ricinine, two extremely toxic proteins (ricin and *Ricinus communis* agglutinin), and 2S albumin storage proteins known to cause immunoglobulin E-mediated immediate hypersensitivity reactions.^{1,2} These allergic reactions have most commonly been due to occupational airborne exposure to castor seed dust, resulting in rhinitis or asthma.³ A combined immediate and delayed cutaneous allergic reaction from castor seed dust has also been observed.^{4,5}

Castor seed oil contains triglycerides with fatty acyl groups composed of approximately 85 to 90% ricinoleic acid. This very high ricinoleic acid content is unique to castor oil, although other plant oils are known to contain smaller quantities.^{6–8} Castor oil also contains smaller amounts of oleic, linoleic, palmitic, and stearic acids.⁹ When the oil is hydrogenated, the ricinoleic acid is converted predominantly to 12-hydroxystearic acid (Fig 1).

There are many reports of allergic contact dermatitis from castor oil^{10–18} and its derivatives, including ricinoleic

acid,^{11,16,19–22} zinc ricinoleate,²³ propylene glycol ricinoleate,²⁴ glyceryl ricinoleate,^{23,25} and sulfated castor oil.²⁶ Sources of exposure have included lip products,^{11,15–17,19–21,24} underarm deodorants,^{23,25} military camouflage,²⁷ wart remover solutions,^{13,14} makeup removers,¹⁸ and lotions or creams.^{10,12}

In contrast, in a search of the PubMed/MEDLINE, EMBASE, and Scopus databases, the author could find only one report each of allergic contact dermatitis from 12-hydroxystearic acid (in lip gloss),²⁸ hydrogenated castor oil (in underarm deodorant),²⁹ and polyethylene glycol-7 hydrogenated castor oil (in sunscreen lotion).³⁰ In addition, there is one report of a patient with contact dermatitis from ricinoleates who had a positive patch-test reaction to hydrogenated castor oil.²⁵ In contrast, two other patients with contact dermatitis from castor oil or ricinoleates had negative patch-test results with hydrogenated castor oil.^{17,23}

Case Report

A 34-year-old male complained of two discrete episodes of lip, face, and eyelid swelling occurring overnight after a single bedtime lip application of Blistex Clear Advance Lip Balm SPF 30 (Blistex, Oak Brook, IL). He had a history of axillary dermatitis from several solid stick underarm antiperspirants and deodorants, including Dove Ultimate Clear Sensitive Skin Fragrance Free Antiperspirant/Deodorant (Unilever, Trumbull, CT). He also had a history of brief dermatitis on the forearms and hands after handling drywall. There was a history of seasonal rhinitis but not of atopic dermatitis.

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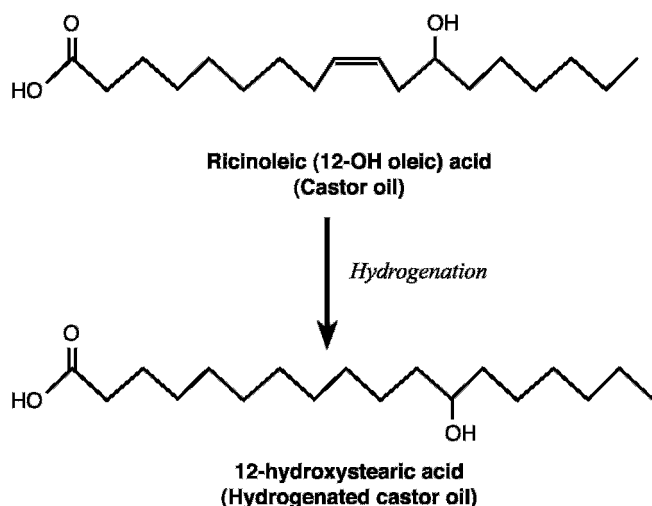


Figure 1. Ricinoleic acid is converted to 12-hydroxystearic acid when castor oil is hydrogenated.

Over 4 years, four series of patch tests were performed with standard polypropylene IQ-Ultra Chambers (Chemotechnique Diagnostics, Vellinge, Sweden) applied to the back (Table 1). Patch tests were occluded for 48 hours and read at 96 or 120 hours. The scoring system was that of the International Contact Dermatitis Research Group (maximum of +++).³¹

The sources and purities of the tested chemicals are noted in the footnotes to Table 1. In particular, highly purified 12-hydroxystearic acid (99.7%) was used for the serial dilution testing. A single unoccluded antecubital application of an extremely small quantity of 12-hydroxystearic acid 10% in petrolatum (pet) caused contact dermatitis within 12 hours (Fig 2). Castor oil 10% pet produced contact dermatitis after 1 week of twice-daily antecubital applications.

The patient has had no further episodes of contact dermatitis after 3 years of avoiding 12-hydroxystearic acid, ricinoleic acid, hydrogenated castor oil, castor oil, and their derivatives.

During the last 3 years, 20 patients with contact dermatitis who were using products containing castor oil, hydrogenated castor oil, or their derivatives were patch tested at the Division of Dermatology of the University of California, San Diego, with castor oil 100%, ricinoleic acid 10% pet, and 12-hydroxystearic acid 10% pet. All of these gave negative patch test results.

Discussion

In a previous analysis of 12-hydroxystearic acid samples used in skin care products, the average purity of the samples was

85%.³² The impurities included stearic acid, palmitic acid, and castor oil triglycerides. Because the 12-hydroxystearic acid test sample supplied to us by the lip balm manufacturer was of unknown purity, subsequent serial dilution testing was performed with 99.7% pure 12-hydroxystearic acid (see Table 1). The positive result at a concentration of 0.001% pet confirms that 12-hydroxystearic acid, not an impurity, is almost certainly the actual allergen. The coexisting patch-test reaction to bis-diglyceryl polyacyladipate-2 (Softisan 649, Sasol North America Inc., Houston, TX), also an ingredient of the lip balm, can be explained by its known content of 12-hydroxystearic acid (see Table 1, footnote 5).³³

The lack of patch-test reactivity to the analogous nonhydroxylated C18 fatty acids—stearic acid and oleic acid (see Table 1)—indicates that hydroxylation was required for allergenicity in this patient.

The patient demonstrated patch-test reactivity to approximately 100-fold lower concentrations of saturated hydroxylated C18 fatty acids (12-hydroxystearic acid and hydrogenated castor oil) as compared to the corresponding unsaturated hydroxylated fatty acids (ricinoleic acid and castor oil) (see Table 1 and Fig 1). This is likely because of differences in the patient's exposure history; he had prolonged exposure to several different solid stick deodorants containing hydrogenated castor oil, but we could not verify previous exposure to castor oil or ricinoleic acid. Alternatively, there could be a difference in the inherent sensitizing capacities of 12-hydroxystearic acid and ricinoleic acid.

As evidenced by the patient's repeated open application test results, his patch-test reaction to castor oil 30% pet was a false-negative reaction. This demonstrates the value of patch-testing with castor oil at full strength,³⁴ which is a nonirritant concentration.^{12,14} Nonetheless, in some cases, even patch tests with full-strength castor oil fail to detect contact allergy to ricinoleic acid or to its salts or esters.^{20,23} This might be due to the limited quantity of free unesterified ricinoleic acid in castor oil. On the other hand, patch-testing with free ricinoleic acid 30% pet was previously shown to cause weak irritant reactions in 5 of 26 controls.¹⁶ For this reason, ricinoleic acid 10% pet was used for the current report. This concentration caused no irritant patch-test reactions in 20 patients.

As with the findings in regard to castor oil, it is possible that allergy to hydrogenated castor oil may not be detected in some patients unless they are tested with 12-hydroxystearic acid. A 12-hydroxystearic acid test concentration of 10% pet did not cause irritant reactions in the 20 patients mentioned above in this report or in 5 patients described in an earlier publication.²⁸

Table 1. Patch-Test Results at Day 5 or Day 6

Allergen	Patch-Test Reactions			
	2005	2006	2007	2008
NACDG* + fragrance + sunscreen series				
p-tert-Butylphenol formaldehyde resin	+			
All others	0			
Blistex Clear Advance Lip Balm SPF 30	++			
Blistex Lip Balm ingredients†				
Hydroxystearic acid 10% pet‡		+++		
Bis-diglyceryl polyacyladipate-2§ 5% pet		+		
Remaining Blistex ingredients (from manufacturer)		0		
Hydroxylated C18 fatty acids				
12-OH, C18:0				
12-hydroxystearic acid 1% pet			++	
12-hydroxystearic acid 0.1% pet			++	
12-hydroxystearic acid 0.01% pet			+	
12-hydroxystearic acid 0.001% pet				+
12-hydroxystearic acid 1% eth			++	
12-hydroxystearic acid 0.1% eth			++	
12-hydroxystearic acid 0.01% eth			0	
Hydrogenated castor oil [¶] 10% pet			++	
Hydrogenated castor oil [¶] 1% pet			+	
12-OH, C18:1, ω9cis				
Ricinoleic acid [#] 10% eth			++	
Ricinoleic acid [#] 1% eth			0	
Ricinoleic acid ^{**} 10% pet				++
Ricinoleic acid ^{**} 1% pet				+
Ricinoleic acid ^{**} 0.1% pet				+
Castor oil 100%				+
Castor oil 30% pet			0	0
Nonhydroxylated fatty acids				
C18:0				
Stearic acid 5% pet, 1% pet, and 2% eth			0	
Glycerol monostearate 10% pet				0
C18:1, ω9cis				
Oleic acid 5% pet			0	
C16:0				
Palmitic acid 5% pet			0	

eth = in ethanol; NACDG = North American Contact Dermatitis Group; pet = in petrolatum.

*Series of 65 allergens.³⁶

†Ingredients supplied courtesy of Blistex (Oak Brook, IL).

‡From Blistex; purity unknown. This lip balm contains 7% 12-hydroxystearic acid.

§The adipic acid diester of a mixed diglyceryl ester of caprylic, capric, stearic, isostearic, and hydroxystearic acids. This lip balm contains 4% bis-diglyceryl polyacyladipate-2.

^{||}From Sigma-Aldrich (St. Louis, MO); 99.7% purity.

[¶]Cutina HR PH, from Cognis Corporation (Monheim, Germany).

[#]From Sigma-Aldrich; 99.5% purity.

^{**}From Spectrum Chemicals and Laboratory Products (Gardena, CA); purity unknown.



Figure 2. A single unoccluded application of a very small quantity of 12-hydroxystearic acid 10% in petrolatum produced contact dermatitis within 12 hours (shown here at 18 hours).

In addition to “hidden” sources such as hydrogenated castor oil and bis-diglyceryl polyacyladipate-1 and -2,³³ there are dozens of other skin care ingredients that are more obvious potential sources of exposure to 12-hydroxystearic acid. Examples include isopropyl hydroxystearate, ethylhexyl hydroxystearate, and trihydroxystearin (a synonym for glyceryl 12-hydroxystearate). In addition to being used in skin care products, hydrogenated castor oil or 12-hydroxystearic acid may be used in topical and oral pharmaceuticals, lubricating oils and greases, paper coating for food packaging, candles, shoe polishes, crayons, pencils, electrical insulation, and many other products.³⁵

Conclusion

This patient experienced contact allergy to saturated and (to a lesser extent) monounsaturated 12-hydroxylated C18 fatty acids. These are respectively present in the greatest quantity in hydrogenated castor oil and in castor oil. The

patient was not allergic to stearic acid or oleic acid, the analogous nonhydroxylated C18 fatty acids.

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